

Poster Session I

none has detectable bcr/abl transcripts in blood or marrow. One patient (CML-CP3) with cytogenetic relapse at D + 118 had a fourth remission after withdrawal of immunosuppression and continued imatinib but developed hematological relapse at D + 429. **Conclusions:** We conclude that imatinib therapy can be safely prescribed early after myeloablative allogeneic HCT at a dose-intensity comparable to that used in general oncology. Preliminary efficacy data are encouraging and worthy of further study (Table1).

Table 1. Patient Characteristics and Outcomes

	ALL (n = 12)	CML (n = 6)
Pretransplant characteristics		
Disease phase, N	CR1 10, CR2 2	AP 2, CP2 2, CP3 2
Patients with MRD ¹ present, N	9	6
Median age, years (range)	36 (5–49)	45 (36–62)
Related donor, unrelated donor, N	5, 7	2, 4
Peripheral blood, marrow, cord blood, N	8, 3, 1	4, 1, 0
Posttransplant outcomes		
Imatinib therapy start day, median (range)	28 (24–39)	29 (25–36)
Imatinib therapy, days of, median (range)	183 (3–381)	243 (89–353)
Average daily imatinib doses, milligrams		
≤Day 90, median (range)	400 (212–400)	400 (no variance)
>Day 90, median (range)	400 (250–550)	400 (no variance)
Survival, days, median (range)	214 (27–600)	511 (130–627)
Molecular remission/completed therapy, N/N		
	4/4	3/4
Molecular remission/continue Imatinib, N/N		
	8/8	2/2

¹MRD = minimal residual leukemia by cytogenetic and/or molecular methods.

²Two children did not receive 400 mg per day but received close to 340 mg/m²/day.

247

DIFFERENCES IN THE PHENOTYPE AND IN VIVO ANTI-TUMOR ACTIVITY OF WT1 SPECIFIC AND EBV-SPECIFIC T-CELLS GENERATED IN VITRO FOR ADOPTIVE IMMUNOTHERAPY

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Our studies in SCID mouse/human tumor xenograft models have demonstrated that T cells sensitized with autologous EBV BLCL in vitro will, following intravenous transfer into mice bearing tumors varying in HLA type and expression of EBV antigens, selectively accumulate in EBV+ tumors co-expressing the T cell's HLA restricting allele, and will proliferate and persist in these tumors through their complete regression. In contrast while T cells sensitized against WT1 peptides presented by peptide-loaded autologous DCs or EBV BLCL in vitro also exhibit HLA-restricted accumulation in WT1+ tumor xenografts and induce significant inhibition of tumor growth, they persist only for periods of 8 days following adoptive transfer. By day 15, the T cells were no longer detectable in the tumors, following which the regrowth of WT1 expressing tumors was again observed. Accordingly, we compared T cells sensitized in vitro with autologous EBV BLCL alone or with EBV BLCL loaded either with the pool of overlapping 15-mers spanning over WT1 sequence or transduced to express WT1. Antigen-specific T cells were then characterized as to their specificity and HLA restriction. Antigen-reactive T cells were then isolated on the basis of IFN γ production in response to secondary restimulation with APCs bearing targeted peptides and the appropriate restricting HLA alleles and evaluated for their phenotype and tumor-specific activity. Both CD4+ and CD8+ EBV-specific T cells exhibited HLA-restricted lysis of EBV+

tumor cells while the CD8+ WT1 specific T cells consistently lysed WT1 tumors bearing HLA restricting HLA class I allele. The CD4+ T cells were not cytotoxic. The WT1-specific and EBV-specific CD4+ T cells did not differ in phenotype. However, while CD8+ T cells specific for EBV expressed an effector memory phenotype (CD3⁺ CD8⁺ CCR7[−] CD45RA⁺ CD45RO⁺ CD62L⁺ CD25⁺), the WT1 specific CD8+ T cells were predominantly of a central memory type (CD3⁺ CD8⁺ CCR7⁺ CD45RA[−] CD45RO⁺ CD62L⁺ CD25⁺). These studies suggest that T cells generated against WT1 in vitro may be relatively deficient in effector memory T cells required to induce complete tumor regression in vivo.

248

HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) FOR MALIGNANCIES USING UMBILICAL CORD BLOOD UNITS (UCB) THAT WERE NOT RED BLOOD CELL DEPLETED

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Cell dosage is a limiting factor for UCB HSCT, especially for adult patients. Most UCB banks practice red cell depletion (RCD) techniques to save storage space, which incur significant nucleated cell loss after processing. One method of minimizing cell loss and still reduce volume after processing is to deplete plasma (PD), but not the red blood cells. Not washing UCB after thawing also minimizes cell loss. A large, racially diverse PD UCB inventory of 18,000 units is now available on stem cell registries. A retrospective analysis was performed on 70 patients with malignancies without prior HSCT who were transplanted during remission with PD UCB. There were 28 ALL, 16 AML, 8 CML, 7MDS/RA/RAEB, 3 JMML, and 8 others. Of the ALL/AML/CML cases with available information, there were 19 1CR/CP, 10 2CR, and 9 3CR/CP. The median age of patients was 5.8 years old (range 0.5–54); median weight 23 kg (range 5–84); male 63%. Transplant characteristics indicated a median # HLA ADR matches of 5.0 (11–6/6; 23–5/6; 27–4/6; 8–/6; 1–/6); median pre-freeze TNC dose 6.4×10^7 /kg; median post-thaw TNC dose as reported by TC 5.3×10^7 /kg; median pre-freeze CD34 dose 2.5×10^5 /kg; transplants outside of U.S. 24%; double unit transplant 14%; non-myeloablative 7%. Forty-seven percent of the transplanted UCB were washed post-thaw (W), 33% were infused without post-thaw wash (NW), with 20% of the units without available post-thaw data. Median time to engraftment for ANC 500 (n = 66), platelet 20K (n = 52), and 50K (n = 50) were 24 days (range 7–49 days), 53 days (range 15–94 days), and 63 days (range 37–132 days), respectively. Median time to engraftment for W versus NW were 28 versus 23 days for ANC500, and 55 versus 49 days for platelet 20K, respectively. The unadjusted cumulative incidence (C.I.) of ANC500 and platelet 20K and 50K engraftments are $93 \pm 3\%$, $76 \pm 6\%$, and $75 \pm 6\%$, respectively. The incidence of reported grade II–IV and III–IV acute GVHD were 37% and 20%, respectively. Twelve percent developed limited chronic GVHD and 15% developed extensive chronic GVHD. With a median follow-up of 282 days (range 50–1263 days), the Kaplan-Meier estimates of 1-year TRM, OS and relapse-free survival were $20 \pm 6\%$, $67 \pm 6\%$, and $59 \pm 7\%$, respectively. These results demonstrate that HSCT using unrelated PD UCB can be performed safely and effectively in patients with malignancies, and post-thaw wash may not be necessary.

249

OUTCOME OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION AFTER ADDING HIGH-DOSE CYTARABINE TO THE CONVENTIONAL Cy/TBI CONDITIONING REGIMEN FOR THE TREATMENT OF PHILADELPHIA-CHROMOSOME-POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA

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